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DATE: Friday, May 14, 2004

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		DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ	
☐	L3	L2 same (pruning or prune or select or selection or deletion or delete)	6
☐	L2	descriptor same nonlinear	31
☐	L1	qsar same nonlinear	3

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Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. Document ID: US 20030220497 A1

L1: Entry 1 of 3 File: PGPB Nov 27, 2003

PGPUB-DOCUMENT-NUMBER: 20030220497
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030220497 A1

TITLE: Novel diflunisal esters and related compounds

PUBLICATION-DATE: November 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hung, Daniel Yung-Yu	Wakerley		AU	
Roberts, Michael Stephen	Westlake		AU	

US-CL-CURRENT: 544/171; 546/237, 548/532, 558/48, 560/34, 560/38, 560/55

ABSTRACT:

O-medium alkyl esters of diflunisal and related compounds are disclosed having anti-platelet activity, hydroxy radical scavenging properties, enhanced hepatic clearance and low ulcerogenic potential. These compounds have general formula (I) wherein n equals 3-13. 1

L1: Entry 1 of 3 File: PGPB Nov 27, 2003

DOCUMENT-IDENTIFIER: US 20030220497 A1
TITLE: Novel diflunisal esters and related compounds

Detail Description Paragraph:
[0287] where k.sub.1, k.sub.2 and k.sub.3 represent the relevant coefficients, C is the ED.sub.50 molar dose and P is the 1-octanol/water partition coefficient. In this work, we found that the more lipophilic esters (longer carbon chain length in O-acyl group) exhibited significantly higher biological activities but a fall off in biological activity as the lipophilicity of this homologous series were higher than C5D. Hence, nonlinear regression analysis was performed using equations (2) and (4) to compute the best correlation between biological activity (log 1/C) and lipophilicity (log P) for this homologous series in determining their optimum QSAR. FIG. 18 shows a parabolic relationship existed between log 1/C and log P for this homologous series. The best correlation obtained is:

☐ 2. Document ID: US 6691045 B1

L1: Entry 2 of 3 File: USPT Feb 10, 2004

US-PAT-NO: 6691045
DOCUMENT-IDENTIFIER: US 6691045 B1

TITLE: Method for determining discrete quantitative structure activity relationships

DATE-ISSUED: February 10, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Labute; Paul R.	Outremont			CA

US-CL-CURRENT: 702/27; 436/43, 436/8, 702/19

ABSTRACT:

Method for developing a quantitative structure activity relationship that includes obtaining a training set of chemical compounds with molecular descriptors consisting of a number of multidimensional vectors with an activity class for each of the vectors; partitioning the multidimensional vectors into groups having interdependence; transforming the descriptors such that the interdependence of the groups is lessened; estimating a probability distribution of the descriptors by assuming that a probability distribution of a product of each of the groups is approximately equal to the probability distribution of the molecular descriptors; performing the partitioning, transforming and estimating steps for each of the activity classes; and, developing a probability distribution for the activity classes.

40 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

L1: Entry 2 of 3 File: USPT Feb 10, 2004

DOCUMENT-IDENTIFIER: US 6691045 B1
TITLE: Method for determining discrete quantitative structure activity relationships

Detailed Description Text (76):
Conventional QSAR based on regression techniques, such as multiple linear regression, partial least squares and, occasionally, neural networks, have been used to cluster compounds. These methods seek to minimize the squared error between the model and the observed data. This optimization of the model parameters introduces sensitivity to errors in experiments and regression analyses. In contrast, binary QSAR does not use any form of regression analysis; there is not attempt to minimize the model errors with regard to model parameters. It is a nonlinear modeling method. Because no regression is used, the model estimation procedure is very fast, which is in contrast to neural networks that require a

lengthy training phase. Therefore, binary QSAR can efficiently process large data sets such as HTS data.

☐ 3. Document ID: US 6593365 B1

L1: Entry 3 of 3 File: USPT Jul 15, 2003

US-PAT-NO: 6593365
DOCUMENT-IDENTIFIER: US 6593365 B1

TITLE: Diflunisal esters and related compounds

DATE-ISSUED: July 15, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Yung-Yu Hung; Daniel	Wakerley			AU
Roberts; Michael Stephen	Westlake			AU

US-CL-CURRENT: 514/533; 514/532, 514/543

ABSTRACT:

O-medium alkyl esters of diflunisal and related compounds are disclosed having anti-platelet activity, hydroxy radical scavenging properties, enhanced hepatic clearance and low ulcerogenic potential. These compounds have general formula (I) wherein n equals 3-13.

4 Claims, 30 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 25

L1: Entry 3 of 3 File: USPT Jul 15, 2003

DOCUMENT-IDENTIFIER: US 6593365 B1
TITLE: Diflunisal esters and related compounds

Detailed Description Text (238):
where k.sub.1, k.sub.2 and k.sub.3 represent the relevant coefficients, C is the ED.sub.50 molar dose and P is the 1-octanol/water partition coefficient. In this work, we found that the more lipophilic esters (longer carbon chain length in O-acyl group) exhibited significantly higher biological activities but a fall off in biological activity as the lipophilicity of this homologous series were higher than C5D. Hence, nonlinear regression analysis was performed using equations (2) and (4) to compute the best correlation between biological activity (log 1/C) and lipophilicity (log P) for this homologous series in determining their optimum QSAR. FIG. 18 shows a parabolic relationship existed between log 1/C and log P for this homologous series. The best correlation obtained is:

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

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Term	Documents
QSAR	627
QSARS	33
NONLINEAR	78621
NONLINEARS	2
(QSAR SAME NONLINEAR).PGPB,USPT,EPAB,JPAB,DWPI.	3
(QSAR SAME NONLINEAR).PGPB,USPT,EPAB,JPAB,DWPI.	3

Display Format: REV,KW Change Format

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Search Results - Record(s) 1 through 6 of 6 returned.

☐ 1. Document ID: US 20020029114 A1

Using default format because multiple data bases are involved.

L3: Entry 1 of 6 File: PGPB Mar 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020029114
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020029114 A1

TITLE: Method, system, and computer program product for detemining properties of combinatorial library products from features of library building blocks

PUBLICATION-DATE: March 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lobanov, Victor S.	Yardley	PA	US	
Agrafiotis, Dimitris K.	Downingtown	PA	US	
Salemme, F. Raymond	Yardley	PA	US	

US-CL-CURRENT: 702/22

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. D

☐ 2. Document ID: US 20010029026 A1

Using default format because multiple data bases are involved.

L3: Entry 2 of 6 File: PGPB Oct 11, 2001

PGPUB-DOCUMENT-NUMBER: 20010029026
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010029026 A1

TITLE: Method and computer program product for designing combinatorial arrays

PUBLICATION-DATE: October 11, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Agrafiotis, Dimitris K.	Downingtown	PA	US	
Lobanov, Victor S.	North Brunswick	NJ	US	

Salemme, Francis R. Yardley PA US

US-CL-CURRENT: 435/7.1; 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 3. Document ID: US 6724925 B2

Using default format because multiple data bases are involved.

L3: Entry 3 of 6 File: USPT Apr 20, 2004

US-PAT-NO: 6724925
DOCUMENT-IDENTIFIER: US 6724925 B2

TITLE: Method and system for the automated delineation of lung regions and costophrenic angles in chest radiographs

DATE-ISSUED: April 20, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Armato, III; Samuel G.	Chicago	IL		
Giger; Maryellen L.	Elmhurst	IL		
MacMahon; Heber	Chicago	IL		

US-CL-CURRENT: 382/132

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 4. Document ID: US 6675103 B1

Using default format because multiple data bases are involved.

L3: Entry 4 of 6 File: USPT Jan 6, 2004

US-PAT-NO: 6675103
DOCUMENT-IDENTIFIER: US 6675103 B1

TITLE: Visualizing high dimensional descriptors of molecular structures

DATE-ISSUED: January 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Patterson; David E.	St. Louis	MO		

US-CL-CURRENT: 702/19; 435/4, 436/501, 702/22, 702/27, 702/30

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw D

☐ 5. Document ID: US 6671627 B2

Using default format because multiple data bases are involved.

L3: Entry 5 of 6 File: USPT Dec 30, 2003

US-PAT-NO: 6671627
DOCUMENT-IDENTIFIER: US 6671627 B2

TITLE: Method and computer program product for designing combinatorial arrays

DATE-ISSUED: December 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Agrafiotis; Dimitris K.	Downingtown	PA		
Lobanov; Victor S.	North Brunswick	NJ		
Salemme; Francis Raymond	Yardley	PA		

US-CL-CURRENT: 702/27; 365/94

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

☐ 6. Document ID: JP 2000276493 A

Using default format because multiple data bases are involved.

L3: Entry 6 of 6 File: JPAB Oct 6, 2000

PUB-NO: JP02000276493A
DOCUMENT-IDENTIFIER: JP 2000276493 A
TITLE: BROWSING METHOD FOR ELECTRONICALLY ACCESSIBLE RESOURCE

PUBN-DATE: October 6, 2000

INVENTOR-INFORMATION:

NAME	COUNTRY
LENNON, ALISON JOAN	

INT-CL (IPC): G06 F 17/30; G06 F 12/00

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Term	Documents
PRUNING	6131
PRUNINGS	160
PRUNE	3215

PRUNES	913
SELECT	792239
SELECTS	338626
SELECTION	775969
SELECTIONS	48810
DELETION	75625
DELETIONS	45773
DELETE	54127
(L2 SAME (PRUNING OR PRUNE OR SELECT OR SELECTION OR DELETION OR DELETE)).PGPB,USPT,EPAB,JPAB,DWPI.	6

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                  CA/CAplus
 NEWS  5  FEB 05  German (DE) application and patent publication number format
                  changes
 NEWS  6  MAR 03  MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03  MEDLINE file segment of TOXCENTER reloaded
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 NEWS  9  MAR 29  Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29  WPIFV now available on STN
 NEWS 11  MAR 29  New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 12  APR 26  PROMT: New display field available
 NEWS 13  APR 26  IFIPAT/IFIUDB/IFICDB: New super search and display field
                  available
 NEWS 14  APR 26  LITALERT now available on STN
 NEWS 15  APR 27  NLDB: New search and display fields available
 NEWS 16  May 10  PROUSDDR now available on STN
 NEWS 17  May 19  PROUSDDR: One FREE connect hour, per account, in both May
                  and June 2004
 NEWS 18  May 12  EXTEND option available in structure searching
 NEWS 19  May 12  Polymer links for the POLYLINK command completed in REGISTRY

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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L1          79 QSAR AND NONLINEAR

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L2          58 DUPLICATE REMOVE L1 (21 DUPLICATES REMOVED)

=> d 1-10 bib ab

L2   ANSWER 1 OF 58     MEDLINE on STN
AN   2004194066     IN-PROCESS
DN   PubMed ID: 15089097
TI   Assessment and modeling of the toxicity of organic chemicals to Chlorella
     vulgaris: development of a novel database.
AU   Cronin Mark T D; Netzeva Tatiana I; Dearden John C; Edwards Robert; Worgan
     Andrew D P
CS   School of Pharmacy and Chemistry, Liverpool John Moores University, Byrom
     Street, Liverpool, L3 3AF, England.. m.t.cronin@livjm.ac.uk
SO   Chemical research in toxicology, (2004 Apr) 17 (4) 545-54.
     Journal code: 8807448. ISSN: 0893-228X.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   IN-PROCESS; NONINDEXED; Priority Journals
ED   Entered STN: 20040420
     Last Updated on STN: 20040513
AB   This study reports a database of toxicity values for 91 compounds assessed
     in a novel, rapid, and economical 15 min algal toxicity test.  The
     toxicity data were measured using the unicellular green alga Chlorella
     vulgaris in an assay that determined the disappearance of fluorescein
     diacetate.  The chemicals tested covered a wide range of physicochemical
     properties and mechanisms of action.  Quantitative activity-activity
     relationships with the toxicity of the chemicals to other species
     (Tetrahymena pyriformis, Vibrio fischeri, and Pimephales promelas) showed
     strong relationships, although some differences resulting from different
     protocols were established.  Quantitative structure-activity relationships
     (QSARs) were determined using linear [multiple linear regression
     (MLR)] and nonlinear [k-nearest neighbors (KNN)] methods.  Three
     descriptors, accounting for hydrophobicity, electrophilicity, and a
     function of molecular size corrected for the presence of heteroatoms, were
     found to be important to model toxicity.  The predictivity of MLR was
     compared to KNN using leave-one-out cross-validation and the simulation of
     an external test set.  MLR demonstrated greater stability in validation.
     The results of this study showed that method selection in QSAR
     is task-dependent and it is inappropriate to resort to more complicated
     but less transparent methods, unless there are clear indications (e.g.,
     inability of MLR to deal with the data set) for the need of such methods.

L2   ANSWER 2 OF 58     MEDLINE on STN
AN   2004053431     MEDLINE
DN   PubMed ID: 14754450
```

TI Neuronal nicotinic acetylcholine receptor agonists: pharmacophores, evolutionary **QSAR** and 3D-**QSAR** models.
AU Nicolotti Orazio; Altomare Cosimo; Pellegrini-Calace Marialuisa; Carotti Angelo
CS Dipartimento Farmaco-Chimico, Universita degli Studi di Bari, Via E. Orabona 4, 70125 Bari, Italy.
SO Current topics in medicinal chemistry, (2004) 4 (3) 335-60. Ref: 132
Journal code: 101119673. ISSN: 1568-0266.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200403
ED Entered STN: 20040203
Last Updated on STN: 20040330
Entered Medline: 20040329
AB Neuronal nicotinic acetylcholine ion channel receptors (nAChRs) exist as several subtypes and are involved in a variety of functions and disorders of the central nervous system (CNS), such as Alzheimer's and Parkinson's diseases. The lack of reliable information on the 3D structure of nAChRs prompted us to focus efforts on pharmacophore and structure-affinity relationships (SAFIRs). The use of DISCO (DIStance COmparison) and Catalyst/HipHop led to the formulation of a pharmacophore that is made of three geometrically unrelated features: (i) an ammonium head involved in coulombic and/or H-bond interactions, (ii) a lone pair of a pyridine nitrogen or a carbonyl oxygen, as H-bond acceptor site, and (iii) a hydrophobic molecular region generally constituted by aliphatic cycles. The quantitative SAFIR (QSAFIR) study was carried out on about three hundred nicotinoid agonists, and coherent results were obtained from classical Hansch-type approach, 3D QSAFIRs, based on Comparative Molecular Field Analysis (CoMFA), and trade-off models generated by Multi-objective Genetic **QSAR** (MoQSAR), a novel evolutionary software that makes use of Genetic Programming (GP) and multi-objective optimization (MO). Within each congeneric series, Hansch-type equations revealed detrimental steric effects as the major factors modulating the receptor affinity, whereas CoMFA allowed us to merge progressively single-class models in a more global one, whose robustness was supported by crossvalidation, high prediction statistics and satisfactory predictions of the affinity data of a true external ligand set (r(2)(pred) = 0.796). Next, MoQSAR was used to analyze a data set of 58 highly active nicotinoids characterized by 56 descriptors, that are log P, MR and 54 low inter-correlated WHIM (Weighted Holistic Invariant Molecular) indices. Equivalent QSAFIR models, that represent different compromises between structural model complexity, fitting and internal model complexity, were found. Our attention was mostly engaged by a number of **nonlinear** QSAFIRs, which relate nAChR affinity with the log P and directional WHIM descriptors. The results reviewed herein show as QSAFIRs may helpfully complement the pharmacophores, thus enhancing the applicability of computer-aided methodologies in the field of nAChR agonists.

L2 ANSWER 3 OF 58 MEDLINE on STN DUPLICATE 1
AN 2004067021 IN-PROCESS
DN PubMed ID: 14768863
TI Predicting toxic equivalence factors from 13C nuclear magnetic resonance spectra for dioxins, furans, and polychlorinated biphenyls using linear and **nonlinear** pattern recognition methods.
AU Buzatu Dan A; Beger Richard D; Wilkes Jon G; Lay Jackson O Jr
CS Division of Chemistry, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, Arkansas 72079, USA.. dbuzatu@nctr.fda.gov
SO Environmental toxicology and chemistry / SETAC, (2004 Jan) 23 (1) 24-31.

Journal code: 8308958. ISSN: 0730-7268.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20040211
Last Updated on STN: 20040211
AB Two quantitative spectrometric data-activity relationships (QSDAR) models have been developed relating 29 dioxin or dioxin-like molecules to their toxic equivalence factors (TEFs). These models were based on patterns in simulated 13C nuclear magnetic resonance (NMR) data with the patterns defined by comparative spectral analysis (CoSA). Two versions of CoSA multiple linear regression (MLR) models using 7 or 10 spectral bins had, respectively, explained variances (r2) of 0.88 and 0.95, and leave-one-out (LOO) cross-validated variances (q2) of 0.78 and 0.88. A third, artificial neural network model--using a feed forward, back propagating, three-layer neural network--produced an r2 of 0.99, a LOO q2 of 0.82, and a leave-three-out q2 of 0.81. A postulated reason that the results of these QSDAR models are better than traditional quantitative structure-activity relationship (**QSAR**) models is based on the difference in descriptors rather than on any differences in pattern recognition approach. Results suggest that the 13C NMR spectral data contain molecular quantum mechanical information more reflective of each molecule's biochemical properties than do the calculated electrostatic potentials and molecular alignment assumptions used in developing **QSAR** models. The QSDAR models provide a rapid, simple way to model the toxicity of dioxin and dioxin-like compounds.

L2 ANSWER 4 OF 58 MEDLINE on STN
AN 2003339406 MEDLINE
DN PubMed ID: 12870926
TI Genetic algorithm applied to the selection of factors in principal component-artificial neural networks: application to **QSAR** study of calcium channel antagonist activity of 1,4-dihydropyridines (nifedipine analogous).
AU Hemmateenejad Bahram; Akhond Morteza; Miri Ramin; Shamsipur Mojtaba
CS Department of Chemistry, Shiraz University, Shiraz, Iran.
SO Journal of chemical information and computer sciences, (2003 Jul-Aug) 43 (4) 1328-34.
Journal code: 7505012. ISSN: 0095-2338.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200312
ED Entered STN: 20030722
Last Updated on STN: 20031218
Entered Medline: 20031211
AB A **QSAR** algorithm, principal component-genetic algorithm-artificial neural network (PC-GA-ANN), has been applied to a set of newly synthesized calcium channel blockers, which are of special interest because of their role in cardiac diseases. A data set of 124 1,4-dihydropyridines bearing different ester substituents at the C-3 and C-5 positions of the dihydropyridine ring and nitroimidazolyl, phenylimidazolyl, and methylsulfonylimidazolyl groups at the C-4 position with known Ca(2+) channel binding affinities was employed in this study. Ten different sets of descriptors (837 descriptors) were calculated for each molecule. The principal component analysis was used to compress the descriptor groups into principal components. The most significant descriptors of each set were selected and used as input for the ANN. The genetic algorithm (GA) was used for the selection of the best set of extracted principal components. A feed forward artificial neural network with a back-propagation of error algorithm was used to process the

nonlinear relationship between the selected principal components and biological activity of the dihydropyridines. A comparison between PC-GA-ANN and routine PC-ANN shows that the first model yields better prediction ability.

L2 ANSWER 5 OF 58 MEDLINE on STN
AN 2003339394 MEDLINE
DN PubMed ID: 12870912
TI Neural networks: Accurate **nonlinear QSAR** model for HEPT derivatives.
AU Douali Latifa; Villemin Didier; Cherqaoui Driss
CS Departement de Chimie, Faculte des Sciences Semlalia BP 2390 Universite Cadi Ayyad, Marrakech, Morocco.. l.douali@ucam.ac.ma
SO Journal of chemical information and computer sciences, (2003 Jul-Aug) 43 (4) 1200-7.
Journal code: 7505012. ISSN: 0095-2338.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200312
ED Entered STN: 20030722
Last Updated on STN: 20031218
Entered Medline: 20031211
AB A **nonlinear** quantitative structure-anti-HIV-1-activity relationship (**QSAR**) study was investigated in a series of 1-[2-hydroxyethoxy-methyl]-6-(phenylthio) thymine] (HEPT) derivatives acting as nonnucleoside reverse transcriptase inhibitors (NNRTIs). This **QSAR** study has been undertaken by a three-layered neural network (NN) using molecular descriptors known to be responsible for the anti-HIV-1 activity. The usefulness of the model and the nonlinearity of the relationship between molecular descriptors and anti-HIV-1 activity have been clearly demonstrated. The obtained model outperforms those given in the literature in both the fitting and predictive stages. NN analysis yielded predicted activities in excellent agreement with the experimentally obtained values (R(2) = 0.977, predictive r(2) = 0.862). The effect of each molecular feature on the anti-HIV-1 activity variation has been clearly elucidated.

L2 ANSWER 6 OF 58 MEDLINE on STN
AN 2003339385 MEDLINE
DN PubMed ID: 12870898
TI Toward generating simpler **QSAR** models: **nonlinear** multivariate regression versus several neural network ensembles and some related methods.
AU Lucic Bono; Nadramija Damir; Basic Ivan; Trinajstic Nenad
CS The Rugjer Boskovic Institute, P.O. Box 180, HR-10002 Zagreb, Croatia.. lucic@irb.hr
SO Journal of chemical information and computer sciences, (2003 Jul-Aug) 43 (4) 1094-102.
Journal code: 7505012. ISSN: 0095-2338.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS PUBMED-NOT-MEDLINE
EM 200312
ED Entered STN: 20030722
Last Updated on STN: 20031218
Entered Medline: 20031211
AB In this study we want to test whether a simple modeling procedure used in the field of **QSAR**/QSPR can produce simple models that will be, at the same time, as accurate as robust Neural Network Ensemble (NNE) ones. We present results of application of two procedures for

generating/selecting simple linear and **nonlinear** multiregression (MR) models: (1) method for selecting the best possible MR models (named as CROMRsel) and (2) Genetic Function Approximation (GFA) method from the Cerius2 program package. The obtained MR models are strictly compared with several NNE models. For the comparison we selected four **QSAR** data sets previously studied by NNE (Tetko et al. J. Chemical Inf. Comput. Sci. 1996, 36, 794-803. Kovalishyn et al. J. Chemical Inf. Comput. Sci. 1998, 38, 651-659.): (1) 51 benzodiazepine derivatives, (2) 37 carboquinone derivatives, (3) 74 pyrimidines, and (4) 31 antimycin analogues. These data sets were parameterized with 7, 6, 27, and 53 descriptors, respectively. Modeled properties were anti-pentylenetetrazole activity, antileukemic activity, inhibition constants to dihydrofolate reductase from MB1428 E. coli, and antifilarial activity, respectively. Nonlinearities were introduced into the MR models through 2-fold and/or 3-fold cross-products of initial (linear) descriptors. Then, using the CROMRsel and GFA programs (J. Chemical Inf. Comput. Sci. 1999, 39, 121-132) the sets of I (I < or = 8, in this paper) the best descriptors (according to the fit and leave-one-out correlation coefficients) were selected for multiregression models. Two classes of models were obtained: (1) linear or **nonlinear** MR models which were generated starting from the complete set of descriptors, and (2) **nonlinear** MR models which were generated starting from the same set of descriptors that was used in the NNE modeling. In addition, the descriptor selection method from CROMRsel was compared with the GFA method included in the **QSAR** module of the Cerius2 program. For each data set it has been found that the MR models have better cross-validated statistical parameters than the corresponding NNE models and that CROMRsel selects somewhat better MR models than the GFA method. MR models are also much simpler than NNEs, which is the important surprising fact, and, additionally, express calculated dependencies in a functional form. Moreover, MR models were shown to be better than all other models obtained by different methods on the same data sets ("old" multivariate regressions, functional-link-net models, back-propagation neural networks, genetic algorithm, and partial least squares models). This study also indicated that the robust NNE models cannot generate good models when applied on small data sets, suggesting that it is perhaps better to apply robust methods (like NNE ones) on larger data sets.

L2 ANSWER 7 OF 58 MEDLINE on STN DUPLICATE 2
AN 2003130918 MEDLINE
DN PubMed ID: 12620084
TI **QSAR** and classification of murine and human soluble epoxide hydrolase inhibition by urea-like compounds.
AU McElroy Nathan R; Jurs Peter C; Morisseau Christophe; Hammock Bruce D
CS Department of Chemistry, 152 Davey Laboratory, The Pennsylvania State University, University Park, Pennsylvania 16802, USA.
NC P30-ESO5707 (NIEHS)
P42-ES04699 (NIEHS)
R37-ES02710 (NIEHS)
SO Journal of medicinal chemistry, (2003 Mar 13) 46 (6) 1066-80.
Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030321
Last Updated on STN: 20030408
Entered Medline: 20030407
AB A data set of 348 urea-like compounds that inhibit the soluble epoxide hydrolase enzyme in mice and humans is examined. Compounds having IC(50) values ranging from 0.06 to >500 microM (murine) and 0.10 to >500 microM (human) are categorized as active or inactive for classification, while

quantitation is performed on smaller compound subsets ranging from 0.07 to 431 microM (murine) and 0.11 to 490 microM (human). Each compound is represented by calculated structural descriptors that encode topological, geometrical, electronic, and polar surface features. Multiple linear regression (MLR) and computational neural networks (CNNs) are employed for quantitative models. Three classification algorithms, k-nearest neighbor (kNN), linear discriminant analysis (LDA), and radial basis function neural networks (RBFNN), are used to categorize compounds as active or inactive based on selected data split points. Quantitative modeling of human enzyme inhibition results in a **nonlinear**, five-descriptor model with root-mean-square errors (log units of IC(50) [microM]) of 0.616 (r(2) = 0.66), 0.674 (r(2) = 0.61), and 0.914 (r(2) = 0.33) for training, cross-validation, and prediction sets, respectively. The best classification results for human and murine enzyme inhibition are found using kNN. Human classification rates using a seven-descriptor model for training and prediction sets are 89.1% and 91.4%, respectively. Murine classification rates using a five-descriptor model for training and prediction sets are 91.5% and 88.6%, respectively.

L2 ANSWER 8 OF 58 MEDLINE on STN
AN 2003173880 MEDLINE
DN PubMed ID: 12692798
TI Selective descriptor pruning for **QSAR**/QSPR studies using artificial neural networks.
AU Turner Joseph V; Cutler David J; Spence Ian; Maddalena Desmond J
CS Faculty of Pharmacy, The University of Sydney, NSW 2006, Australia.. jvturner@pharm.usyd.edu.au
SO Journal of computational chemistry, (2003 May) 24 (7) 891-7.
Journal code: 9878362. ISSN: 0192-8651.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS PUBMED-NOT-MEDLINE
EM 200312
ED Entered STN: 20030416
Last Updated on STN: 20031217
Entered Medline: 20031202
AB Selection of optimal descriptors in quantitative structure-activity-property relationship (**QSAR**/QSPR) studies has been a perennial problem. Artificial Neural Networks (ANNs) have been used widely in **QSAR**/QSPR studies but less widely in descriptor selection. The current study used ANNs to select an optimal set of descriptors using large numbers of input variables. The effects of clean, noisy, and random input descriptors with linear, **nonlinear**, and periodic data on synthetic and real data **QSAR**/QSPR sets were examined. The optimal set of descriptors could be determined using a signal-to-noise ratio method. The optimal values for the rho parameter, which relates sample size to network architecture, were found to vary with the type of data. ANNs were able to detect meaningful descriptors in the presence of large numbers of random false descriptors.

L2 ANSWER 9 OF 58 MEDLINE on STN DUPLICATE 3
AN 2003208803 MEDLINE
DN PubMed ID: 12729701
TI Separation of the strength and selectivity of the microbiological effect of synthetic dyes by spectral mapping technique.
AU Oros Gyula; Cserhati Tibor; Forgacs Esther
CS Plant Protection Institute, Hungarian Academy of Sciences, 1022 Herman O. 15, Budapest, Hungary.
SO Chemosphere, (2003 Jul) 52 (1) 185-93.
Journal code: 0320657. ISSN: 0045-6535.
CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200306
ED Entered STN: 20030506
Last Updated on STN: 20030625
Entered Medline: 20030624
AB The growth inhibitory effect of 30 synthetic dyes on 22 bacteria (test organisms) belonging to various taxonomic groups was determined. The strength (potency) and selectivity of the biological effect were separated by the spectral mapping technique, reducing the dimensionality of the selectivity maps to two by the **nonlinear** mapping technique. The relationship between biological effect and physicochemical parameters of dyes was elucidated by stepwise regression analysis. It has been established that the strength of the effect of anthracene and trityl derivatives was higher than that of azobenzene dyes and significantly depended on the hydrophobicity of the compound. The selectivity of the effect also depended on hydrophobicity and on the nonpolar unsaturated surface area of the dyes. Gram negative and Gram positive bacteria differed in the strength and selectivity of their response to dyes indicating the marked impact of the taxonomical position on the response. Contrary to other multivariate mathematical statistical methods biological activity may be divided by SPM into potency and selectivity values, therefore, application of the technique in future **QSAR** studies is highly recommended.

L2 ANSWER 10 OF 58 MEDLINE on STN DUPLICATE 4
AN 2002672119 MEDLINE
DN PubMed ID: 12408718
TI Multiobjective optimization in quantitative structure-activity relationships: deriving accurate and interpretable **QSARs**.
AU Nicolotti Orazio; Gillet Valerie J; Fleming Peter J; Green Darren V S
CS Krebs Institute for Biomolecular Research and Department of Information Studies, University of Sheffield, Western Bank, United Kingdom.
SO Journal of medicinal chemistry, (2002 Nov 7) 45 (23) 5069-80.
Journal code: 9716531. ISSN: 0022-2623.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200212
ED Entered STN: 20021116
Last Updated on STN: 20021217
Entered Medline: 20021209
AB Deriving quantitative structure-activity relationship (**QSAR**) models that are accurate, reliable, and easily interpretable is a difficult task. In this study, two new methods have been developed that aim to find useful **QSAR** models that represent an appropriate balance between model accuracy and complexity. Both methods are based on genetic programming (GP). The first method, referred to as genetic **QSAR** (or GPQSAR), uses a penalty function to control model complexity. GPQSAR is designed to derive a single linear model that represents an appropriate balance between the variance and the number of descriptors selected for the model. The second method, referred to as multiobjective genetic **QSAR** (MoQSAR), is based on multiobjective GP and represents a new way of thinking of **QSAR**. Specifically, **QSAR** is considered as a multiobjective optimization problem that comprises a number of competitive objectives. Typical objectives include model fitting, the total number of terms, and the occurrence of **nonlinear** terms. MoQSAR results in a family of equivalent **QSAR** models where each **QSAR** represents a different tradeoff in the objectives. A practical consideration often overlooked in **QSAR** studies is the need for the model to promote an understanding

of the biochemical response under investigation. To accomplish this, chemically intuitive descriptors are needed but do not always give rise to statistically robust models. This problem is addressed by the addition of a further objective, called chemical desirability, that aims to reward models that consist of descriptors that are easily interpretable by chemists. GPQSAR and MoQSAR have been tested on various data sets including the Selwood data set and two different solubility data sets. The study demonstrates that the MoQSAR method is able to find models that are at least as good as models derived using standard statistical approaches and also yields models that allow a medicinal chemist to trade statistical robustness for chemical interpretability.

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=> d his

     (FILE 'HOME' ENTERED AT 14:08:39 ON 14 MAY 2004)

     FILE 'MEDLINE, BIOSIS' ENTERED AT 14:08:51 ON 14 MAY 2004
L1            79 S QSAR AND NONLINEAR
L2            58 DUPLICATE REMOVE L1 (21 DUPLICATES REMOVED)

=> s l2 and py<2002
L3            40 L2 AND PY<2002

=> s l3 and (descriptor (3A) (prun? or select? or delet?))
L4             2 L3 AND (DESCRIPTOR (3A) (PRUN? OR SELECT? OR DELET?))

=> d 1-2 bib ab

L4   ANSWER 1 OF 2     MEDLINE on STN
AN   2000184551     MEDLINE
DN   PubMed ID: 10719637
TI   A comparative QSAR study of benzamidines complement-inhibitory
     activity and benzene derivatives acute toxicity.
AU   Basak S C; Gute B D; Lucic B; Nikolic S; Trinajstic N
CS   Natural Resources Research Institute, University of Minnesota, Duluth
     55811, USA.
SO   Computers & chemistry, (2000 Mar) 24 (2) 181-91.
     Journal code: 7607706. ISSN: 0097-8485.
CY   ENGLAND: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200004
ED   Entered STN: 20000505
     Last Updated on STN: 20000505
     Entered Medline: 20000421
AB   A novel QSAR study of benzamidines complement-inhibitory
     activity and benzene derivatives acute toxicity is reported and a new
     efficient method for selecting descriptors is used.
     Complement-inhibitory activity QSAR models of benzamidines
     contain from one to five descriptors. The best, according to fitted and
     cross-validated statistical parameters, is shown to be the five-descriptor
     model. Models with a higher number of indices did not improve over the
     five-descriptor model. The benzene derivatives structure-toxicity models
     involve up to seven linear descriptors. Multiregression models,
     containing up to ten nonlinear descriptors, are also reported
     for the sake of comparison with previously obtained additivity models.
     Comparison with benzamidine complement-inhibitory activity models and with
     benzene derivatives toxicity models from the literature favors our novel
     approach.

L4   ANSWER 2 OF 2  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
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AN 2000:386660 BIOSIS
DN PREV200000386660
TI Quantitative structure-activity relationship (**QSAR**) study of flavonoid derivatives for inhibition of cytochrome P450 1A2.
AU Moon, Taesung; Chi, Myung Hwan; Kim, Dong-Hyun; Yoon, Chang No [Reprint author]; Choi, Young-Sang
CS Bioanalysis and Biotransformation Research Center, Korea Institute of Science and Technology, Cheongryang, Seoul, 130-650, South Korea
SO Quantitative Structure-Activity Relationships, (June, 2000) Vol. 19, No. 3, pp. 257-263. print.
CODEN: QSARDI. ISSN: 0931-8771.
DT Article
LA English
ED Entered STN: 13 Sep 2000
Last Updated on STN: 8 Jan 2002
AB The quantitative structure-activity relationships (**QSAR**) studies on flavonoid derivatives as cytochrome P450 1A2 inhibitors were performed using multiple linear regression analysis (MLR) and neural networks (NN). The results of MLR and NN show that Hammett constant, the highest occupied molecular orbital energy (HOMO), the nonoverlap steric volume, the partial charge of C3 carbon atom, and the HOMO pi coefficients of C3, C3' and C4' carbon atoms of flavonoids play an important role in inhibitory activity. The correlations between the descriptors and the activities were improved by neural networks although the descriptors of optimum MLR model were used in the networks, which implies that the descriptors used in MLR model include **nonlinear** relationships. Moreover, neural networks using **descriptors selected** by the **pruning** method gave higher r2 value than neural networks using MLR descriptors.

=> d his

(FILE 'HOME' ENTERED AT 14:08:39 ON 14 MAY 2004)

FILE 'MEDLINE, BIOSIS' ENTERED AT 14:08:51 ON 14 MAY 2004
L1 79 S QSAR AND NONLINEAR
L2 58 DUPLICATE REMOVE L1 (21 DUPLICATES REMOVED)
L3 40 S L2 AND PY<2002
L4 2 S L3 AND (DESCRIPTOR (3A) (PRUN? OR SELECT? OR DELET?))

=> s l3 and descriptor not l4
L5 14 L3 AND DESCRIPTOR NOT L4

=> d 1-14 bib ab

L5 ANSWER 1 OF 14 MEDLINE on STN
AN 2001557246 MEDLINE
DN PubMed ID: 11604021
TI Toward an optimal procedure for variable selection and **QSAR** model building.
AU Yasri A; Hartsough D
CS Computational Design Group, ArQule Inc., 19 Presidential Way, Woburn, MA 01801, USA.. ayasri@arqule.com
SO Journal of chemical information and computer sciences, **(2001 Sep-Oct)** 41 (5) 1218-27.
Journal code: 7505012. ISSN: 0095-2338.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011018
Last Updated on STN: 20020122

Entered Medline: 20011207

AB In this work, we report the development of a novel **QSAR** technique combining genetic algorithms and neural networks for selecting a subset of relevant **descriptors** and building the optimal neural network architecture for **QSAR** studies. This technique uses a neural network to map the dependent property of interest with the **descriptors** preselected by the genetic algorithm. This technique differs from other variable selection techniques combining genetic algorithms to neural networks by two main features: (1) The variable selection search performed by the genetic algorithm is not constrained to a defined number of **descriptors**. (2) The optimal neural network architecture is explored in parallel with the variable selection by dynamically modifying the size of the hidden layer. By using both artificial data and real biological data, we show that this technique can be used to build both classification and regression models and outperforms simpler variable selection techniques mainly for **nonlinear** data sets. The results obtained on real data are compared to previous work using other modeling techniques. We also discuss some important issues in building **QSAR** models and good practices for **QSAR** studies.

L5 ANSWER 2 OF 14 MEDLINE on STN

AN 2001450301 MEDLINE

DN PubMed ID: 11495588

TI Adaptive neuro-fuzzy inference system: an instant and architecture-free predictor for improved **QSAR** studies.

AU Loukas Y L

CS Department of Pharmaceutical Chemistry, School of Pharmacy, University of Athens, Panepistimiopolis, Zografou, 157 71 Athens, Greece.. loukas@pharm.uoa.gr

SO Journal of medicinal chemistry, **(2001 Aug 16)** 44 (17) 2772-83. Journal code: 9716531. ISSN: 0022-2623.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200109

ED Entered STN: 20010813
Last Updated on STN: 20010910
Entered Medline: 20010906

AB The application of an adaptive neuro-fuzzy inference system (ANFIS) has been developed for obtaining sufficient quantitative structure-activity relationships (**QSAR**) with high accuracy. To this end, a data set of 68 pyrimidines derivatives as DHFR inhibitors, described first in the excellent independent studies of Hansch et al. (J. Med. Chemical 1982, 25, 777-784 and J. Med. Chemical 1991, 34, 46-54) and later by So and Richards (J. Med. Chemical 1992, 35, 3201-3207), was examined. The ANFIS system, first time applied in the literature to **QSAR** studies, was trained using a hybrid algorithm consisting of back-propagation and least-squares estimation while the optimum number and shape of membership functions were obtained through the subtractive clustering algorithm. Prior to the development and evaluation of the ANFIS system, geometry optimization of the examined compounds was performed, deriving a series of diverse **descriptors** from which the best subset was selected by using a hybrid genetic algorithm system. The predictive abilities of the resulting models compared to those produced from classical multivariate regression such as linear and **nonlinear** (quadratic) partial least squares regression (PLS and QPLS, respectively). The ANFIS method outperformed both the PLS models as well as the published results, leading to substantial gain in both the prediction ability and the computation speed (almost instant training).

L5 ANSWER 3 OF 14 MEDLINE on STN

AN 2001365812 MEDLINE
DN PubMed ID: 11410051
TI Classification of environmental estrogens by physicochemical properties using principal component analysis and hierarchical cluster analysis.
AU Suzuki T; Ide K; Ishida M; Shapiro S
CS Chemical Resources Laboratory, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503, Japan.. tsuzuki@res.titech.ac.jp
SO Journal of chemical information and computer sciences, **(2001 May-Jun)** 41 (3) 718-26.
Journal code: 7505012. ISSN: 0095-2338.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726
AB A structurally diverse assortment of 60 environmental estrogens was divided into two main clusters ("A", "B") and a pair of subclusters ("C1", "C2") by applying principal component analysis to selected 1D and 2D molecular **descriptors** and subjecting the PCs to hierarchical cluster analysis. Although clustering was predicated solely on physicochemical properties, the dependence on particular physicochemical parameters of xenoestrogen binding affinities (pK(i)) to murine uterine cytosolic estrogen receptor (ER) proved greater for compounds within (sub)clusters than for compounds between (sub)clusters. Quantitative structure-binding affinity relationships derived using molecular **descriptors** and PCs suggested differences in the driving forces for xenoestrogen-ER binding for different (sub)clusters. The modeling power for xenoestrogen-ER binding affinities of a combination of TLSER and WHIM 3D indices was much greater than that of combinations of 1D and 2D molecular **descriptors** or the PCs derived therefrom. The clusterings obtained using PCs also proved applicable to the 3D-**QSARs**.

L5 ANSWER 4 OF 14 MEDLINE on STN
AN 2001313946 MEDLINE
DN PubMed ID: 11386859
TI Mathematical programming assisted drug design for nonclassical antifolates.
AU Garg S; Achenie L E
CS Department of Chemical Engineering, University of Connecticut, Storrs, Connecticut 06269, USA.
SO Biotechnology progress, **(2001 May-Jun)** 17 (3) 412-8.
Journal code: 8506292. ISSN: 8756-7938.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20011022
Last Updated on STN: 20011022
Entered Medline: 20011018
AB A concept from optimization theory, specifically, mathematical programming, is proposed for designing drugs with desired properties. The mathematical programming formulation is solved to obtain the optimal **descriptor** values, which are employed in the Cerius(2) modeling environment to infer the optimal lead candidates, in the sense that they exhibit both high selectivity and activity while ensuring low toxicity. It has been observed that unique substituent groups and their molecular conformations are responsible for attaining the goal of simultaneous high selectivity and activity. Both linear and **nonlinear**

quantitative structure activity relationships (**QSARs**) have been developed for use in the proposed approach. A comparative study of these models is done, and it is shown that the **QSARs** are well represented by **nonlinear** models. The proposed mathematical programming strategy has been demonstrated for a class of nonclassical antifolates for Pneumocistis carinii and Toxoplasma gondii dihydofolate reductase. Some of the potential leads found in this study have biological properties similar to those in the open literature. We believe the technique proposed is general and can be applied to other structure based drug design.

L5 ANSWER 5 OF 14 MEDLINE on STN
AN 2000299724 MEDLINE
DN PubMed ID: 10840686
TI Toward minimalistic modeling of oral drug absorption.
AU Oprea T I; Gottfries J
CS AstraZeneca R&D Molndal, Sweden.. tudor.oprea@astrazeneca.com
SO Journal of molecular graphics & modelling, **(1999 Oct-Dec)** 17 (5-6) 261-74, 329.
Journal code: 9716237. ISSN: 1093-3263.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200007
ED Entered STN: 20000714
Last Updated on STN: 20000714
Entered Medline: 20000706
AB Poor intestinal permeability of drugs constitutes a major bottleneck in the successful development of candidate drugs. Fast computational tools to help in designing compounds with increased probability of oral absorption are required, since both medicinal and combinatorial chemists are under pressure to consider increasing numbers of virtual and existing compounds. The **QSAR** paradigm for drug absorption is expressed as a function of molecular size, hydrogen-bonding capacity, and lipophilicity. A **nonlinear** PLS model that can be achieved with minimal computational efforts is described. The **QSAR** model correlates human intestinal absorption (%HIA) data, and apparent Caco-2 cell permeability data, to parameters calculated from molecular structures. Two properties were found to be relevant for absorption predictions, namely H-bonding capacity, and hydrophobic transferability. The parsimony principle was applied in several aspects: single conformers were used to compute molecular surface areas; the definitions of "polar" and "nonpolar" surfaces were done in a simplistic fashion; simple and fast 2D **descriptors** were used to estimate other properties; the 1 PLS component model was selected. These choices result in a minimalistic model for oral absorption. The use of both %HIA and Caco-2 permeability data was found to stabilize and improve the model. This **QSAR** model can serve as a simple, quantitative extension of the "rule of five" scheme (Lipinski, C.A., Lombardo, F., Dominy, B.W., and Feeney, P.J. Adv. Drug Deliv. Rev. 1997, 23, 3-25), in a manner that can prove beneficial to the drug discovery process.

L5 ANSWER 6 OF 14 MEDLINE on STN
AN 1999339881 MEDLINE
DN PubMed ID: 10409408
TI Prediction of fathead minnow acute toxicity of organic compounds from molecular structure.
AU Eldred D V; Weikel C L; Jurs P C; Kaiser K L
CS Department of Chemistry, 152 Davey Laboratory, The Pennsylvania State University, University Park, Pennsylvania 16802, USA.
SO Chemical research in toxicology, **(1999 Jul)** 12 (7) 670-8.
Journal code: 8807448. ISSN: 0893-228X.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
ED Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819
AB Interest in the prediction of toxicity without the use of experimental data is growing, and quantitative structure-activity relationship (**QSAR**) methods are valuable for such predictions. A **QSAR** study of acute aqueous toxicity of 375 diverse organic compounds has been developed using only calculated structural features as independent variables. Toxicity is expressed as -log(LD(50)) with the units -log(millimoles per liter) and ranges from -3 to 6. Multiple linear regression and computational neural networks (CNNs) are utilized for model building. The best model is a **nonlinear** CNN model based on eight calculated molecular structure **descriptors**. The root-mean-square log(LD(50)) errors for the training, cross-validation, and prediction sets of this CNN model are 0.71, 0.77, and 0.74 -log(mmol/L), respectively. These results are compared to a previous study with the same data set which included many more **descriptors** and used experimental data in the **descriptor** pool.

L5 ANSWER 7 OF 14 MEDLINE on STN
AN 96417513 MEDLINE
DN PubMed ID: 8820304
TI Variable mapping of structure-activity relationships: application to 17-spirolactone derivatives with mineralocorticoid activity.
AU Grassy G; Trape P; Bompart J; Calas B; Auzou G
CS Center de Biochimie Structurale, Universite de Montpellier 1, Faculte de Pharmacie, France.
SO Journal of molecular graphics, **(1995 Dec)** 13 (6) 356-67.
Journal code: 9014762. ISSN: 0263-7855.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970313
Last Updated on STN: 19970313
Entered Medline: 19970305
AB Fifty-four steroid homologs, belonging to the series of 17-spirolactones, were modelled by molecular and quantum mechanics. We studied the affinity of these compounds for the cytosolic mineralocorticoid receptor by way of various parameters describing each structure and its molecular properties. After the failure of a classic preliminary **QSAR** study, demonstrating the **nonlinear** relationships between affinity and structural **descriptors**, we constructed a model allowing us to predict the affinity of new compounds. Our method is based on simple graphic tools coupled to a cluster significance analysis. A complementary study of the activity relating the prediction of the antagonist/agonist character of 37 high-affinity compounds was also carried out using the same methodology. The principal electronic and structural characteristics leading to a selective activity were revealed.

L5 ANSWER 8 OF 14 MEDLINE on STN
AN 96382766 MEDLINE
DN PubMed ID: 8790630
TI Application of neural networks in the **QSAR** analysis of percent effect biological data: comparison with adaptive least squares and **nonlinear** regression analysis.
AU Wiese M; Schaper K J

CS Forschungsinstitut Borstel, Med.-Pharm. Chemie, Borstel, Germany.
SO SAR and QSAR in environmental research, **(1993)** 1 (2-3) 137-52.
Journal code: 9440156. ISSN: 1062-936X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 19961106
Entered Medline: 19961021
AB Artificial neural networks (ANN) can be used for the direct **QSAR** analysis of percent effect biological data, thus avoiding the bias introduced by arbitrarily chosen classes and the loss of information due to prior classification. For two data sets the ANN results are compared with those obtained by adaptive least squares and **nonlinear** regression analyses. In comparison with the other methods the neural network shows higher predictive power and does not require an explicit equation relating the observed effect to physicochemical **descriptors.**

L5 ANSWER 9 OF 14 MEDLINE on STN
AN 96382764 MEDLINE
DN PubMed ID: 8790628
TI How to see characteristics of structural parameters in **QSAR** analysis: **descriptor** mapping using neural networks.
AU Ichikawa H; Aoyama T
CS Hoshi College of Pharmacy, Tokyo, Japan.
SO SAR and QSAR in environmental research, **(1993)** 1 (2-3) 115-30.
Journal code: 9440156. ISSN: 1062-936X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 19961106
Entered Medline: 19961021
AB In addition to its outstanding abilities in both classification and fitting, the neural network can also accurately predict the values of the untrained region. To rationalize this ability of prediction, the authors mathematically discussed the valid region of prediction. Based on such a background, the authors proposed "**descriptor** mapping" in the **QSAR** analysis, which visualizes the **nonlinear** dependencies between structural parameters. A variable of the linear multiple regression analysis in the **QSAR** study is supposed to be linear to the biological intensity and is independent of other variables. Analysis by the **descriptor** mapping method discloses the reality.

L5 ANSWER 10 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1997:505531 BIOSIS
DN PREV199799804734
TI **Nonlinear** CoMFA using QPLS as a novel 3D-**QSAR** approach.
AU Hasegawa, Kiyoshi; Kimura, Toshiro; Funatsu, Kimito [Reprint author]
CS Dep. Knowledge-Based Inf. Eng., Toyohashi Univ. Technol., Tempaku-cho, Toyohashi 441, Japan
SO Quantitative Structure-Activity Relationships, (1997) Vol. 16, No. 3, pp. 219-223.
CODEN: QSARDI. ISSN: 0931-8771.
DT Article
LA English
ED Entered STN: 21 Nov 1997

Last Updated on STN: 21 Nov 1997
AB Comparative molecular field analysis (CoMFA) using partial least squares (PLS) is a popular method in 3D-**QSAR** studies. Although CoMFA has been of general use, it is suboptimal or even useless when **nonlinear** relationships are observed between field variables and biological activity. Quadratic PLS (QPLS) developed by Wold et al. is an extension of PLS to deal with **nonlinear** chemical data. In this paper, it is demonstrated that QPLS can be applicable to the 3D field variables in CoMFA. The structure-activity data of dihydrofolate reductase (DHFR) inhibitors were used as a test example. The resulting QPLS model gave high predictivity with only one component to explain the **nonlinear** relationships between the electrostatic field variables and inhibitory activity. The loading values of the QPLS model were plotted in 3D space and chemically reasonable contour maps were obtained in accordance with the previous multiple and non-linear regression (MLR) model.

L5 ANSWER 11 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1995:433629 BIOSIS
DN PREV199598447929
TI Artificial neural network studies in quantitative structure-activity relationships of antifungal azoxy compounds.
AU Hasegawa, K.; Deushi, T.; Yaegashi, O.; Miyashita, Y. [Reprint author]; Sasaki, S.
CS Dep. Knowledge-Based Information Eng., Toyohashi Univ. Technol., Tempaku-cho, Toyohashi 441, Japan
SO European Journal of Medicinal Chemistry, (1995) Vol. 30, No. 7-8, pp. 569-574.
CODEN: EJMCA5. ISSN: 0223-5234.
DT Article
LA English
ED Entered STN: 10 Oct 1995
Last Updated on STN: 10 Oct 1995
AB Artificial neural networks (ANN) based on the back-propagation algorithm (BP algorithm) were applied to a quantitative structure-activity relationship (**QSAR**) study for 30 azoxy compounds with antifungal activity. The ANN model could well explain the variance of the antifungal activity owing to its ability to deal with a **nonlinear** tendency in the data set. A modified BP algorithm proposed by the authors has provided the ANN model with a more enhanced predictive capability. Finally, a transformation of the final ANN model to a polynomial of original physico-chemical parameters was shown to be useful to elucidate the structural requirements for the antifungal activity.

L5 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1993:47604 BIOSIS
DN PREV199395023906
TI 3D-quantitative structure-activity relationships: **Nonlinear** dependence described directly from 3D structures using a comparative molecular field analysis (CoMFA) approach.
AU Kim, Ki Hwan
CS Computer Assisted Mol. Design Pharmaceutical Products Div., Abbott Labs., Abbott Park, Ill. 60064, USA
SO Quantitative Structure-Activity Relationships, (1992) Vol. 11, No. 3, pp. 309-317.
CODEN: QSARDI. ISSN: 0931-8771.
DT Article
LA English
ED Entered STN: 13 Jan 1993
Last Updated on STN: 13 Jan 1993
AB The applicability of the comparative molecular field analysis (CoMFA) approach to describe the parabolic or bilinear dependence of biological activity on hydrophobicity in 3D quantitative-structure-activity

relationships (**QSAR**) has been investigated. Molecular fields calculated with a H-20 probe produced significant correlations with excellent cross-validation. The results indicate that the CoMFA approach is an excellent methodology for describing **nonlinear** effects in 3D **QSAR** studies.

L5 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1992:429163 BIOSIS
DN PREV199294081288; BA94:81288
TI APPLICATION OF FUNCTIONAL-LINK NET IN **QSAR** 1. **QSAR** FOR ACTIVITY DATA GIVEN BY CONTINUOUS VARIATE.
AU LIU Q [Reprint author]; HIRONO S; MORIGUCHI I
CS SCH PHARMACEUTICAL SCIENCES, KITASATO UNIV, SHIROKANE, MINATO-KU, TOKYO 108, JAPAN
SO Quantitative Structure-Activity Relationships, (1992) Vol. 11, No. 2, pp. 135-141.
CODEN: QSARDI. ISSN: 0931-8771.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 22 Sep 1992
Last Updated on STN: 22 Sep 1992
AB We attempted to apply a new pattern recognition method called "functional-link net" (Klassen and Pao, 1988) to **QSAR**. In contrast to the linear weighting produced by the generalized delta rule net often used in neural nets, the functional-link net acts on a pattern element (a structural parameter in **QSAR**) or on the entire pattern itself to generate a set of **nonlinear** functions. In usual **QSAR** studied, linear forms of parameters are generally used. But, in many cases, parameters might contribute semilinearly to activity. Such a semilinear contribution of parameters can be examined by semilinearly transforming the parameters into a new parameter vector using a procedure with the architecture of the functional-link net. The new method presented here was devised for analysis of **QSAR** from activity data given by a continuous variate. The application of this method to **QSAR** of several data sets of carboquon analogues with antileukemic activity gave better results than those given by multiple regression analysis of the same data sets. The comparison of the results with those given by the generalized delta rule net also showed that FUNCLINK was superior in the predictive ability.

L5 ANSWER 14 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1990:351863 BIOSIS
DN PREV199090048442; BA90:48442
TI QUATERNARY AMMONIUM SALTS XXXIII **QSAR** OF ANTIMICROBIALLY ACTIVE NIKETHAMIDE DERIVATIVES.
AU DEVINSKY F [Reprint author]; LACKO I; MYLNARCIK D; SVAJDLENKA E; BOROVSKA V
CS DEP INORGANIC AND ORGANIC CHEM, LAB BIOORGANIC CHEM, FAC PHARM, COMENIUS UNIV, CS 832 32 BRATISLAVA
SO Chemical Papers, (1990) Vol. 44, No. 2, pp. 159-170.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 7 Aug 1990
Last Updated on STN: 23 Sep 1990
AB Quantitative structure-activity relationships (**QSAR**) for 13 1-alkyl-3-(N,N-diethylcarbamoyl)pyridinium bromides are reported. Effect of the alkyl chain length (m) variation upon antimicrobial activity against S. aureus, E. coli, and C. albicans, respectively, expressed as minimum inhibitory concentration (MIC) and upon critical micellar concentration (Ck) which was taken as a measure of lipophilicity of the compounds was followed. **Nonlinear** relationships between MIC vs.

m and Ck were quantified using a parabola and the bilinear model. The bilinear dependence describes better the experimentally found data and the optimum values for Ck calculated from these regression equations show that only compounds with Ck in a certain narrow range around 1 mmol dm-3 will exhibit maximum antimicrobial activity regardless of microorganism strain used in the tests. This maximum is related to compounds containing 15 to 17 carbon atoms in their long alkyl chain.

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E1          37     EWING T/AU
E2           3     EWING T A/AU
E3           6 --> EWING T J/AU
E4           1     EWING T J A/AU
E5          16     EWING T L/AU
E6           5     EWING T M/AU
E7           2     EWING T N/AU
E8           1     EWING T R/AU
E9           1     EWING T W/AU
E10          4     EWING THOMAS L/AU
E11          1     EWING TODD/AU
E12          9     EWING TODD J A/AU

=> s e4
L6           1 "EWING T J A"/AU

=> d bib ab

L6   ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN   1999:87979  BIOSIS
DN   PREV199900087979
TI   CombiDOCK: Structure-based combinatorial docking and library design.
AU   Sun, Y. [Reprint author]; Ewing, T. J. A.; Skillman, A. G.;
     Kuntz, I. D. [Reprint author]
CS   Dep. Pharm. Chem., Univ. Calif., San Francisco, CA 94143-0446, USA
SO   Journal of Computer-Aided Molecular Design, (Nov., 1998) Vol. 12, No. 6,
     pp. 597-604. print.
     CODEN: JCADEQ. ISSN: 0920-654X.
DT   Article
LA   English
ED   Entered STN: 1 Mar 1999
     Last Updated on STN: 1 Mar 1999
AB   We have developed a strategy for efficiently docking a large combinatorial
     library into a target receptor. For each scaffold orientation, all
     potential fragments are attached to the scaffold, their interactions with
     the receptor are individually scored and factorial combinations of
     fragments are constructed. To test its effectiveness, this approach is
     compared to two simple control algorithms. Our method is more efficient
     than the controls at selecting best scoring molecules and at selecting
     fragments for the construction of an exhaustive combinatorial library. We
     also carried out a retrospective analysis of the experimental results of a
     10 X 10 X 10 exhaustive combinatorial library. An enrichment factor of
     approximately 4 was found for identifying the compounds in the library
     that are active at 330 nM.

=> s e3
L7           6 "EWING T J"/AU

=> s l7 and qsar
L8           0 L7 AND QSAR

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---Logging off of STN---

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	32.25	32.46

STN INTERNATIONAL LOGOFF AT 14:21:34 ON 14 MAY 2004